## REMARKS

Claims 8, 14, and 36 have been amended. Claims 8, 14, 15, 22, 33, 34, and 36-38 are pending. No new matter has been introduced herewith. The following addresses the substance of the Final Office Action.

**Claim rejections under 35 U.S.C. §112**

The Examiner has maintained rejections of Claims 8, 14, 15, 22 and has further rejected Claims 33, 34, and 36-38 under 35 U.S.C. §112, first paragraph as allegedly lacking enablement. More specifically, the Examiner believes that even though the human parkin2 shares a high percentage of sequence similarity with the mouse homologue, whether the mouse Parkin2 comprising the same mutation as the human would produce the same Parkinson's symptoms is unpredictable because the genetic control elements and genetic backgrounds of human and rodent are very different. The Examiner has invited the Applicant to provide recent references that teach the phenotype of one transgenic specie is predictable of the same phenotype of another specie (i.e. from human to mouse). The Applicant has now provided such references. See, for example, Aponte J.L. et al. 2001, *PNAS USA* **98**:641-645 (Appendix 1); Sommer G. et al. 2003 *PNAS USA* **100**:6706-6711 (Appendix 2); Olsson J.E. 1992 *Neuron* **9**:815-830 (Appendix 3); Barlow C. et al. 1996 *Cell* **86**:159-171 (Appendix 4); Peters T. et al 2003 *Hum. Mol. Genet.* **12**:2109-2120 (Appendix 5); "HHMI News: Researchers Develop Mouse Model of Rett Syndrome" 2002 (Appendix 6); "HHMI News: Building a Better Mouse Model for Lung Cancer", 2001 (Appendix 7); Sommer et al WO 98/03644 (Appendix 8); and McConlogue et al. USP 5,612,486 (Appendix 9). In fact, The Jackson Laboratory provides commercially more than 100 mouse/human gene homologs strains (see Appendix 10); at least two International Mouse genome Conferences: in 2002 and 2003 were devoted to mouse models of human disease (see Appendices 11 and 12).

The Examiner has also maintained that the Specification is not enabling for making a transgenic rat comprising mouse parkin2 mutation, because the references provided in the response to the previous Office Action filed April 25, 2003 do not teach generation of a transgenic rat involving rat embryonic stem cells. The Applicants now provide new references to show that generation of a transgenic rat using embryonic stem cells was known at the time this

invention was made. See, for example, USP 6,156,952 (e.g., 15:8-12) (Appendix 13), and USP 6,372,956 (e.g., 14:19-24) (Appendix 14).

The Examiner has rejected Claims 8, 14, 15, 22, 33, 34, 36-38 under 35 U.S.C. §112, first paragraph for allegedly lacking the written description. More specifically, the Examiner argues that the definition of a "homologue" of the mouse mutant parkin2 gene is lacking and that the Specification fails to describe a representative number of species by their complete structure or other identifying characteristics. The Applicant has amended the independent Claims 8, 14 and 36 to specify the definition of a homolog as "a homolog of said mutant mouse parkin2 protein wherein said homolog has an amino acid sequence having at least 70% amino acids identical to said mutant mouse parkin2 protein", as supported by the Specification as filed on page 7, lines 19-29. Therefore, the Applicant respectfully asserts that Claims 8, 14, 15, 22, 33, 34, and 36-38 are now enabled and withdrawal of the rejection of these claims is specifically requested.

The Examiner has rejected Claim 14 under 35 U.S.C. §112, second paragraph for omitting essential steps of how to produce a transgenic mouse or rat from the chimeric mouse or rat. More specifically, the Examiner has indicated that the method claim must include all essential steps and refer back to the preamble. Accordingly, Applicant has now amended Claim 14 to add such a step. Therefore, Claim 14 is now deemed complete and in condition for allowance.

For all of the above reasons, Applicants respectfully request withdrawal of all rejections under 35 U.S.C. § 112, and allowance of the pending application.

## CONCLUSION

Applicants have endeavored to address all of the Examiner's concerns as expressed in the outstanding Final Office Action. Accordingly, amendments to the claims, the reasons therefor, and arguments in support of the patentability of the pending claim set are presented above. In light of the above amendments and remarks, reconsideration and withdrawal of the outstanding rejections is specifically requested. If the Examiner finds any remaining impediment to the prompt allowance of these claims that could be clarified with a telephone conference, the Examiner is respectfully requested to initiate the same with the undersigned.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: 2/4/04

By: _____

Mark Benedict
Registration No. 44,531
Attorney of Record
Customer No. 20,995
(949) 760-0404

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